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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,877	03/05/2002	Philip T. Feldsine	150026.457C1	7854

500 7590 12/28/2005

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EXAMINER

WINKLER, ULRIKE

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 12/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/091,877	Applicant(s) FELDSINE ET AL.	
	Examiner Ulrike Winkler	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 October 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 3, 4 and 27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 4, 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The Amendment filed October 5, 2005 in response to the Office Action of April 5, 2005 is acknowledged and has been entered. Claims 1, 3, 4 and 27 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 3, 4 and 27 under 35 U.S.C. 103(a) as being unpatentable over Deng et al. (Antimicrobial Agents and Chemotherapy, 1995), Marino et al. (Journal of Bacteriology 1991, see IDS) and Ohyama et al. (Journal of Bacteriology 1992, see IDS) is **maintained** for reasons of record. The rejection is evidenced by the Handbook: Microbiological Media (Ronald M., 1997, CRC Press Inc. Boca Raton, FL, pp 1113, 1349,1482, 1491, 1492) and Ferguson et al. (Journal of Bacteriology, 1978). The following references have been added as further evidence showing as showing that the ordinary artisan would appreciate that a change in the outer surface membrane of a bacteria will effect the immunogenicity of the bacteria. Principles of Microbiology. (10th ed. S.D. Schapper editor, Times Mirror/Mosby College Publishing (1984) page 31), McDermid et al. (Infection and Immunity (1993) Vol. 61, No. 5, pages 1743-1749), Judd et al. (Molecular Microbiology (1989), Vol. 3, No. 5, pageds 637-643).

Applicants arguments is that it would not be common knowledge that a change in the composition of a bacterial cell wall would result in a change in the antigenicity of the bacterial cell wall surface. "Applicants note that none of the cited references discuss antigenicity of

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bacterial cell walls, and the Action provides no other documentary evidence for this allegation.”

In response the following evidentiary references are cited for the common knowledge that the bacterial cell wall determines the antigenicity of the bacteria and that alteration in the structure and composition of the cell wall has an effect on the antigenicity of the organism:

Judd et al. Topographical alterations in proteins I of *Neisseria gonorrhoeae* correlated with lipooligosaccharide variation. *Molecular Microbiology* (1989), Vol. 3, No. 5, pages 637-643.

Judd et al. determined that the antigenicity of a protein 1 subclass A (P.1A) or protein 1 subclass (P.1B) is dependent on the presence and expression of a lipooligosaccharide (LOS) and H.8 antigen. The presence of the LOS on the cell surface may mask the epitopes of protein 1 or other outer membrane proteins

McDermid et al. Effect of growth condition on expression and antigenicity of staphylococcus epidermis RP62A cell envelope proteins. *Infection and Immunity* (1993) Vol. 61, No. 5, pages 1743-1749.

McDermid et al. looked at varying growth conditions for *Staphylococcus epidermis* and found that under certain conditions some antigens are either not expressed or not recognized by the antiserum (see Table 2).

In response to applicant's argument that “Applicants submit one of ordinary skill in the art would not be motivated to include Tween in a low-density bacterial culture because clumping is scarce or non-existent.” The fact that applicant has recognized another advantage of a detergent (Tween) in a cell culture which would flow naturally following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). The use of detergents such as

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Tween in bacterial cell culture is well known (see Ronald M., Handbook: microbiological media pp 1113, 1349, 1482, 1491, 1492), Tween not only acts to prevent cell clumping but it can also act as an additional energy source for some bacteria (Ferguson et al. Journal of Bacteriology, 1978). Deng et al. teaches incubating a bacterial cell in the presence of a detergent (Tween) and a structure modifying organic compound (ethambutol) and observes changes in the cell surface lipopolysaccharide structures.

The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Deng et al. incubated mycobacteria in the presence of Tween and a structure modifying organic compound, the reference specifically looked at the effects on the cell wall composition, indicating that the bacterial cell wall is modified. The use of detergents such as Tween in bacterial cell culture is well known (see Ronald M., Handbook: microbiological media pp 1113, 1349, 1482, 1491, 1492), Tween not only acts to prevent cell clumping but it can also act as an additional energy source for some bacteria (Ferguson et al. Journal of Bacteriology, 1978). Marino et al. treated cells with DNP and observed the changes in the cell wall composition, indicating that the structure of the bacterial cell wall has been modified. So both the Deng et al. reference and the Marino et al. reference provide bacterial incubation methods that alters the structure of the cell wall. The ordinary artisan would recognize that alteration of a bacterial cell wall would have an effect on the antigenicity of the cell. "It is prima facie obvious

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to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted).

The limitation "permitting multiplication to optimal levels for detection" is interpreted as an intended use limitation. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and In re Otto, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). The intended use of achieving optimum growth levels for detection would not effect the composition.

The instant invention is drawn to a composition comprising a general enrichment media including a detergent and at least one structure modifying organic chemical, and a method of propagating the microorganism. Wherein the structure modifying compound is selected from 2,4-dinitrophenol (DNP) or carbonyl cyanide-m-chlorophenyl hydrazone.

Deng et al. teaches the culturing of *Mycobacterium smegmatis* in glycol-alanine-salts medium in the presence of Tween 80 and ethambutol, a structure modifying compound (see page 696, paragraph spanning column 1 and 2). The reference teaches the growth of a bacteria in a general enrichment medium containing a detergent (Tween-80) in the presence of a structure modifying organic chemical, ethambutol. The reference teaches that the incubation of the

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bacteria in the presence of the structure modifying organic compound results in a change in the cell wall composition (see figure 4 and table 1). Ethambutol inhibits biosynthesis of arabinan in lipoarabinomannan, a lipopolysaccharide, that is associated with the cell wall. The reference does not disclose incubating the microorganism using 2,4-dinitrophenol (DNP) or carbonyl cyanide-m-chlorophenyl hydrazone. The reference does not test for antigenic changes in the cell wall in response to the treatment with the structure modifying organic chemical, ethambutol.

Marino et al. teach incubating microorganism in growth medium (PPBE) and 1 mM 2,4-dinitrophenol (DNP). Addition of high concentrations of DNP completely blocked the subsequent translocation of lipopolysaccharide to the outer membrane (results page 14966). The LPS does not reach the outer membrane after incubation with DNP (see figure 3, and table 1). The reference also looks at the translocation of LPS in the presence of CCCP (see table 2). The reference teaches the localization of LPS after treatment with a structure modifying organic compositions. Here the structure modifying organic composition had the effect of inhibiting the transport of the lipopolysaccharide to the outer membrane.

Ohyama et al. teach incubating microorganism in growth medium in the presence of carbonyl cyanide-m-chlorophenyl hydrazone (CCCP).

It would have been obvious to one of ordinary skill in the art to add a detergent to the growth medium comprising a microorganism in order to avoid the clumping of the microorganism as set out in Deng et al. The use of detergents such as Tween in bacterial cell is well known (see Ronald M., Handbook: microbiological media pp 1113, 1349, 1482, 1491, 1492), Tween not only acts to prevent cell clumping but it can also act as an additional energy source for some bacteria (Ferguson et al. Journal of Bacteriology, 1978). One having ordinary

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skill in the art would have had a high expectation of success in adding the detergent to the procedures set out in Ohyama et al. or Marino et al. Therefore, the instant invention would have been obvious over Deng et al., Marino et al. and Ohyama et al.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action (See MPEP 2144.04 D). Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (571) 273-8300.


Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.


ULRIKE WINKLER, PH.D.
PRIMARY EXAMINER

12/23/05